

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000054409	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2004/003224	International filing date (day/month/year) 26.03.2004	Priority date (day/month/year) 31.03.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant UNIVERSITY OF BRISTOL		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>12</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input checked="" type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-105 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. 1-26 _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* _____ received by this Authority on _____
- nos.* _____ received by this Authority on _____
- ☒ the drawings:
- sheets 1/37-37/37 _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) -- see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. IV

Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:

see Supplemental Box

4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-11 (in part), 15-26 (in part)

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-11	YES
	Claims	15-26	NO
Inventive step (IS)	Claims		YES
	Claims	1-26	NO
Industrial applicability (IA)	Claims	1-26	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

1. This report makes reference to the following documents; the same numbering will be used throughout the procedure and corresponds to their order of appearance in the international search report:

D1: WO0159128 (BASF AG)
D2: Alonso and Maroto, 2000; Biotechnol. Advan.
18: 481-497
D3: WO02072742 (Bertholed et alia)
D4: WO0018889 (Calgene)

2. **PCT Article 33(2) and 33(3) (novelty and inventive step)**

- 2.1 Claim 11 relates to a derivative of SEQ. ID. No. 1 which codes for an amino acid sequence having at least 40% homology (sic) to SEQ. ID. No. 2. D4 (SEQ. ID. NO. 6) discloses an amino acid sequence having 44.9% **identity** with SEQ. ID. No. 2. The corresponding nucleic acid (SEQ. ID. No. 5) falls under the subject matter of claim 11 and is therefore not novel under EPC Article 54. This

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

also applies to dependent claims 15-23.

2.2 Should the applicant succeed in re-establishing formal novelty, attention should be paid to paragraph 2.6.

2.3 Claim 1 relates to a process for producing polyunsaturated fatty acids using nucleic acid sequences as also defined in claim 11.

There are no convincing indications, either in the prior art or in the description, that a sequence which is a derivative of SEQ. ID. No. 1 and codes for a polypeptides with only 40% homology (sic) with the SEQ. ID. No. 2 could solve the problem addressed in claim 1, namely the production of polyunsaturated fatty acids in an organism. The functional limitation, "equivalent lysophosphatidic acid acyltransferase activity", which is more than unclear, does not remedy this defect.

2.4 The International Searching Authority assumes that only a sequence which codes for a polypeptide having a much greater **identity** and a clear functional limitation could solve the stated problem.

2.5 Consequently, claim 1 does not meet the requirements of PCT Article 33(3). This also applies to dependent claims 2-10.

2.6 This argument also applies to the subject matter of claim 11(c). This claim, as well as dependent

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>claims 15-23, also fail to meet the requirements of PCT Article 33(3).</p> <p>2.7 Claim 24 relates to oils, lipids or fatty acids produced by a process as per one of the claims 12-21. This type of claim is admissible only when the product obtained by the process, i.e. the oils, lipids or fatty acids, meet the patentability requirements.</p> <p>2.8 This does not appear to be the case, since documents D1-D3 disclose oils, lipids or fatty acids which deprive the subject matter of claim 24 of novelty. Claim 24 does not meet the requirements of PCT Article 33(2). This also applies to claims 25 and 26, which relate to corresponding oil, lipid and fatty acid compositions, as well as to their use.</p>

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

This report was based on the sequence listing on pages 1-120 of the description as originally filed.

* If item 4 in Box No. 1 applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

BOX IV.3**Lack of unity of invention**

1. PCT Article 3(4)(iii) and Rule 13.2 stipulate that when a group of inventions is claimed, the requirement for unity of invention is met only when a technical relationship involving one or more of the same or corresponding special technical features exists between these inventions.
2. The term "special technical features" designates the technical features which characterise in each claim the contribution of the claimed invention as a whole over the prior art.
3. The only technical feature which links all the different groups of inventions in the application is that they all relate to acyltransferases specific to the transfer of long-chain, polyunsaturated fatty acids. However, these acyltransferases are already known in the prior art (e.g. WO0018889; Zou *et alia*, 1999; Hobbs *et alia*, 1999; Knutzon *et alia*, 1995; Lassner *et alia*, 1995). This technical relationship therefore does not constitute a contribution over the prior art which links the different inventions in such a way that they form a single general inventive concept.

Supplemental Box

4. The only technical feature that links inventions 1-12 is that they relate to a 1-acylglycerin-3-phosphate acyltransferase (lysophosphatidic acid acyltransferase, EC 2.3.1.51). However, this acyltransferase was also already known in the prior art (e.g. Knutzon *et alia*, 1995). Consequently, this technical relationship also fails to constitute a contribution over the prior art which links the twelve inventions in such a way that they form a single general inventive concept.
5. The only technical feature that links inventions 13-15 is that they relate to a glycerin-3-phosphate acyltransferase (EC 2.3.1.15). However, this acyltransferase was also already known in the prior art (e.g. EMBL AF090734). Consequently, this technical relationship also fails to constitute a contribution over the prior art which links the three inventions in such a way that they form a single general inventive concept.
6. The only technical feature that links inventions 16-18 is that they relate to a diacylglycerin acyltransferase (EC 2.3.1.20). However, this acyltransferase was also already known in the prior art (e.g. Hobbs *et alia*, 1999; Zou *et alia*, 1999). Consequently, this technical relationship also fails to constitute a contribution over the prior art which links the three inventions in such a way that they form a single general inventive concept.

Supplemental Box

7. The only technical feature that links inventions 19-20 is that they relate to a lecithin cholesterin acyltransferase (EC 2.3.1.43). However, this acyltransferase was also already known in the prior art (e.g. McLean *et alia*, 1986). Consequently, this technical relationship also fails to constitute a contribution over the prior art which links the three inventions in such a way that they form a single general inventive concept.
8. Consequently, the application lacks unity of invention, and the different inventions which do not share a common inventive concept have been separated into different groups (PCT Article 17(3)(a)).
- 8.1 **Invention 1:** claims 1-11 (in part), 15-26 (in part), which relate to a 1-acylglycerin-3-phosphate acyltransferase from *Thraustochytrium* (SEQ. ID. No. 2) and the corresponding nucleic acid (SEQ. ID. No. 1), constructs and organisms which contain the corresponding nucleic acid, process for producing polyunsaturated fatty acids using the acyltransferase, the thus produced oils, lipids and fatty acids, as well as the use of these oils, lipids and fatty acids.
- 8.2 **Inventions 2-12:** claims 1-11 (in part), 15-26 (in part); like invention 1, but relating to 1-acylglycerin-3-phosphate acyltransferases of SEQ.

Supplemental Box

ID. No. 3, 4, 6, 7, 9, 11, 13, 14, 16, 18, 20
(nucleic acids) and 5, 8, 10, 12, 15, 17, 19, 21
(polypeptides).

8.3 **Invention 13:** claims 1-10 (in part), 12 (in part),
15-26 (in part), which relate to a glycerin-3-
phosphate acyltransferase from *Physcomitrella*
(SEQ. ID. No. 23) and the corresponding nucleic
acid (SEQ. ID. No. 22), constructs and organisms
which contain the corresponding nucleic acid,
process for producing polyunsaturated fatty acids
using the acyltransferase, the thus produced oils,
lipids and fatty acids, as well as the use of
these oils, lipids and fatty acids.

8.4 **Inventions 14 and 15:** claims 1-10 (in part), 12
(in part), 15-26 (in part); like invention 13, but
relating to glycerin-3-phosphate acyltransferases
of SEQ. ID. No. 24, 26 (nucleic acids) and 25, 27
(polypeptides).

8.5 **Invention 16:** claims 1-10 (in part), 13 (in part),
15-26 (in part), which relate to a diacylglycerin
acyltransferase from *Cryptocodinium* (SEQ. ID. No.
29) and the corresponding nucleic acid (SEQ. ID.
No. 28), constructs and organisms which contain
the corresponding nucleic acid, process for
producing polyunsaturated fatty acids using the
acyltransferase, the thus produced oils, lipids
and fatty acids, as well as the use of these oils,
lipids and fatty acids.

Supplemental Box

- 8.6 **Inventions 17 and 18:** claims 1-10 (in part), 13 (in part), 15-26 (in part); like invention 16, but relating to diacylglycerin acyltransferases of SEQ. ID. No. 30, 32 (nucleic acids) and 31, 33 (polypeptides).
- 8.7 **Invention 19:** claims 1-10 (in part), 14 (in part), 15-26 (in part), which relate to a lecithin cholesterin acyltransferase from *Physcomitrella* (SEQ. ID. No. 34) and the corresponding nucleic acid (SEQ. ID. No. 35), constructs and organisms which contain the corresponding nucleic acid, process for producing polyunsaturated fatty acids using the acyltransferase, the thus produced oils, lipids and fatty acids, as well as the use of these oils, lipids and fatty acids.
- 8.8 **Invention 20:** claims 1-10 (in part), 14 (in part), 15-26 (in part), which relate to a lecithin cholesterin acyltransferase from *Fusarium* (SEQ. ID. No. 34) and the corresponding nucleic acid (SEQ. ID. No. 35), constructs and organisms which contain the corresponding nucleic acid, process for producing polyunsaturated fatty acids using the acyltransferase, the thus produced oils, lipids and fatty acids, as well as the use of these oils, lipids and fatty acids.